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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/190,887	11/12/98	CORMIER M	ARC2589CIP1

022921
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HM12/0912

EXAMINER	
CELSA, B	
ART UNIT	**PAPER NUMBER**
1627	11

DATE MAILED: 09/12/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File copy

Office Action Summary

Application No.	Applicant(s)
09/190,887	Cormier et al.
Examiner	**Group Art Unit**
Bennett Celsa	1627

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-20* is/are pending in the application.

Of the above, claim(s) *9-20* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-8* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4 and 5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Status of the Claims

Claims 1-20 are currently pending.

Claims 1-8 are under consideration.

Claims 9-20 are withdrawn from consideration as being directed to a nonelected invention.

1. Applicant's election of hGH and Gly-His in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the election of species requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Applicant's election with traverse of Group I (claims 1-8) in Paper No. 9 is acknowledged. Applicant amended claim 12 to recite a new method and accordingly the following substitute restriction requirement in response to applicant's amendment follows:

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-8, drawn to dipeptide containing compositions, classified, for example, in class 260, subclass 998+.

II. Claims 9-11, drawn to a transdermal delivery apparatus, classified, for example, in class 128 , subclass 200+ .

III.. Claims 12-20, drawn to a method of making a transdermal electrotransport delivery formulation of a drug or electrolyte, classified, for example, in class 514 , subclass 2+; class 604, subclass 20+.

3. The inventions are distinct, each from the other because of the following reasons: Inventions I and II are drawn to totally different classes of inventions (e.g. composition v. apparatus) and the apparatus vis a vis the composition has different modes of operation, different functions, or different effects and need not employ the composition of Group I.

4. Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the process for using the product as claimed can be practiced with another materially different product(s) such as the use of amino acid buffers or use of "classic buffers" (e.g. TRIS) as buffering agents (e.g. see specification pages 3-5) to effect electrotransport delivery of a drug and. (2) the product as claimed can be used in a materially different process of using that product such as the formulation of a drug composition with dipeptide buffers for parenteral delivery. .

5. Inventions II and III are drawn to totally different classes of inventions (e.g. apparatus v. method) in which the method does not necessitate the use of the apparatus and vice versa.

6. Because these inventions are distinct for the reasons given above and

a. have acquired a separate status in the art as shown by their different classification;

b. require different and separately burdensome manual/computer name, classification and bibliographic searches; and

c. because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

7. Applicant's election with traverse of Group I (claims 1-8) in Paper No. 9 is acknowledged. The traversal is on the ground(s) that "the Examiner has not cited support for the restriction between the composition claims of Group I and the device claims of Group II (claims 9-11). " This is not found persuasive since reasons were given in item 1. (Page 2) of the previous response e.g. that Group I and II are drawn to different classes of inventions (apparatus v. Composition) wherein the apparatus has different modes of operation and does not require the composition; and additionally groups I and II (in item 4.) are drawn to different classifications (e.g. class 260 v. Class 128); require different and separately burdensome searches and are drawn to divergent subject matter.

Applicant further argues that MPEP section 806.05c does not support restriction. However, MPEP 806.05c drawn to restriction between combination and subcombination is only applicable within the same class of invention e.g. a composition comprising A and a composition comprising A and B. In the present case MPEP 806.05c is not applicable since claims drawn to a composition and claims drawn to an apparatus represent different invention classes. Additionaly, ample reasons were provided for restricting between the device and the composition claims.

Turning to the restriction between Group I and Group III applicant argues that the amended claims of Group III must be viewed as a process of making the composition of Group I which renders Groups I and III non-restrictable..

The Examiner respectfully disagrees.

The Group III invention is drawn to a method of making an electrotransport composition and thus is drawn to a means of use of the Group I composition. Accordingly, the Examiner has provided two separate justifications for restriction of Group III from Group I e.g. different compositions can be employed for electrotransport delivery; and the composition of claim 1 can be used in a totally unique manner e.g. parenterally delivery.

Additionally, restriction between Group I and III can be further justified since these groups:

a. have acquired a separate status in the art as shown by their different classification;

b. require different and separately burdensome manual/computer name, classification and bibliographic searches; and

c. because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper. In this regard, a reference drawn to the same composition of Group I will be anticipatory; regardless of the reference use; since the composition of Group I recites "intended use language". With regard to Group III claims 12 and 20 require that electrotransport delivery be considered; which is not necessary for the Group I invention.

Applicant further argues that MPEP 809.03 "Linking Claims" mandates that Groups I, II and III be considered together. However, the Examiner does not see a claim(s) that are "inseparable therefrom and thus linking" as recited in the MPEP section. In fact, the Examiner has provided ample evidence regarding why and how Groups I and III are properly restrictable.

However, it is noted that in accordance with U.S. practice, upon the allowance of a compound claim within an elected compound invention (e.g. Group I), the Examiner will *consider rejoinder of* method of use claims and conventional apparatus claims that comprisethe novel composition (e.g. Groups II and III) which are commensurate in scope to the allowed subject matter pursuant to MPEP 821.04 Rejoinder

Accordingly, the requirement, as modified in response to applicant's amendment, is still deemed proper and is therefore made FINAL.

Oath/Declaration (objection)

8. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It was not executed in accordance with either 37 CFR 1.66 or 1.68. One of the inventors (e.g. Iris Leung) has not signed.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claim 1, use of the term "drug" and "electrolyte" in the alternative is confusing since some drugs are electrolytes in solution and some electrolytes are classifiable as drugs. Accordingly, the term "drug" and "electrolyte" are not mutually exclusive.

Additionally, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation "drug" , and the claim also recites "electrolyte" which is the narrower statement of the range/limitation.

B. In claim 1, the following phrase is not understood: "the dipeptide buffer comprising a polypeptide chain of 2 to 5 amino acids". If the term "dipeptide" present in the phrase "dipeptide

buffer" is being described as "a polypeptide chain of 2 to 5 amino acids" then it is confusing as to how a dipeptide can contain 3-5 amino acids and still be a dipeptide. Another possible interpretation of the phrase "the dipeptide buffer comprising a polypeptide chain of 2 to 5 amino acids" is that the buffer contains two peptides one of which is a dipeptide and the other of which is a polypeptide of 2-5 amino acids. However, the specification appears to lack any specification support. Clarification is respectfully requested.

C. In claim 1, the term "dipeptide buffer" is confusing as to whether this is addressing *a single compound* (e.g. one dipeptide) which acts as a buffer; or whether "dipeptide buffer" is drawn to a buffer composition which comprises a dipeptide and additional ingredients. Clarification is requested.

D. In claim 1, the phrase "the dipeptide having at least 2 pKa's which are separated by no more than about 3.5 pH units" lacks metes and bounds since the pK of a given dipeptide will vary given the particular selected dipeptide and the experimental conditions for measuring pH. Accordingly, defining the dipeptide by its pKA lacks metes and bounds since the claim neither recites the conditions present for determining pH or the particular dipeptide.

E. In claim 3, the phrase " dipeptide is present ... at a concentration of at least about 10mM" is indefinite since the solution volume which is necessary for determining the concentration of dipeptide e.g. (mMoles/liter) is not present in the claim.

11. It is noted that the present application is a CIP of 08/969,217 (filed 11/12/97). The presently claimed invention contains new matter (e.g. isoelectric pH and Pka limitations) which is

not supported in the previous 08/969,217 application. Accordingly, priority under 35 USC 120 for the presently claimed invention is hereby denied; and the claimed invention is afforded the filing date of the present application (e.g. 11/12/98) for purposes of prior art.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to

the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-2 and 4-7 are rejected under 35 U.S.C. 102(b) as being anticipated or in the alternative as being prima facie obvious over Stover et al., , J. Chromat. Vol. 470 (5/89) pages 241-50..

Stover et al. disclose compositions comprising deionized water and aqueous buffer solutions of pH 6-9 comprising "electrolytes" (e.g. Kcl, MES: see Table 1 and page 243) and a histidine derivative e.g. Gly-His (e.g. see Table II) on page 244 A pH between 6-9 is "within about 1.0 pH unit of the isoelectric pH" of Gly-His which is 7.5. Additionally, Gly-His inherently has "an isoelectric pH at which the dipeptide carries no net charge". Accordingly, the reference composition contains all of the required components in the requisite amounts of claim 1. Intended use language "for transdermal electrotransport delivery" is not given patentable weight in the a composition or compound claim. Alternatively, the use of "electrophoretic buffer solutions" (e.g. see page 242) would "immediately envisage" (e.g. anticipate) the use of the resulting compositions for transdermal electrotransport delivery or in the alternative render such use prima facie obvious.

15. Claims 1-8 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Sorensen WO 93/12812 (7/93)..

Sorensen disclose pharmaceutical compositions that comprise hGH at pH 6.5 containing His containing dipeptides, including His-Gly at a concentration of 10mM; and an electrolyte (e.g. phosphate) . See Examples 1-6 and claims 1-9. Intended use language "for transdermal electrotransport delivery" is not given patentable weight in the a composition or compound claim. A pH of 6.5 is "within about 1.0 pH unit of the isoelectric pH" of the disclosed reference histidine containing dipeptides, including His-Gly.

To the extent that the reference fails to teach the use of Gly-His as the His containing dipeptide such a selection would be immediately envisaged (e.g. anticipated) or in the alternative prima facie obvious given the reference teaching of the use of any His containing dipeptides; the exemplification of His-Gly as one of the preferred dipeptides; and the small number of possible His containing dipeptides available for selection (e.g. see the reference on page 15, lines 16-24. See *In re Schaumann*, 572 F.2d 312. 197 USPQ 5 (CCPA 1978). Additionally, the reference dipeptide ranges e.g. 5-25 mM; 5-15 mM (e.g. see page 12, lines 19-22) would immediately envisage (e.g. anticipate) or alternatively render obvious (via optimization) the presently claimed dipeptide range of "at least about 10mM.

16. Claims 1-8 are rejected under 35 U.S.C. 102(a, b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bjorn et al. WO 97/397,768 (10/97).

The Bjorn et al. Reference discloses pharmaceutical aqueous compositions comprising: a growth hormone (preferably hGH), a Histidine dipeptide comprising X-His or His-X (where X is one of the 19 remaining naturally occurring alpha amino acids) in a concentration of .about .01-about 10 mg/mg of GH in a pH of "about 6- about 8.8". See Abstract; pages 10-13 ; and claims. The dipeptide concentration amounts, and the pH are within the scope of the presently claimed invention (e.g. between "about 3 and 10" for the dipeptide; and "pH is within about 1.0 ph unit of the isoelectric pH). Intended use language "for transdermal electrotransport delivery" is not given patentable weight in the a composition or compound claim. Accordingly, the reference anticipates present claims 1-5, 7 and 8.

To the extent that the reference fails to teach the use of Gly-His as the His containing dipeptide such a selection would be immediately envisaged (e.g. anticipated) or in the alternative prima facie obvious given the reference teaching of the use of any His containing dipeptide of X-His or His-X formulas; the exemplification of His-Gly as one of the preferred dipeptides (e.g. see page 15, lines 25-30); and the small number of possible His containing dipeptides available for selection (e.g. see the reference on page 15, lines 16-24. See *In re Schaumann*, 572 F.2d 312. 197 USPQ 5 (CCPA 1978).

Additionally, the reference further anticipates or alternatively renders obvious the presence of "electrolytes" within the scope of the presently claimed invention (e.g. the selection of natrium chloride as an isotonicity agent) . See claims 25 and 26

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat (art unit 1627), can be reached at (703)308-0570.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1627)

September 8, 2000

BENNETT CELSA
PRIMARY EXAMINER